REMARKS

Claims 97, 99, and 105-113 are pending. Claims 97, 99, 112 and 113 have been amended. No new matter has been introduced by the current amendment, which more specifically and clearly describes the claimed subject matter.

Double Patenting

Applicants thank the Examiner for withdrawing the rejection for obviousness-type double patenting over claims 1-18 of US 5,656,593, claims 1-29 of US 5,733,878, claims 1-14 of US 6,333,312, claims 1-25 of US 6,281,195, claims 1-20 of US 5,972,884, claims 1-24 of US 5,739,107, claims 1-19 of US 5,849,686, claims 1-5 of US 6,531,445, claims 1-8 of US 6,399,569, claims 1-8 of 6,936,582.

In addition, rejection over claims 1-30 of US 5,674,844 pertaining to bone loss, as stated by Examiner Turner in the May 18, 2006 Office Action was not addressed in the present Office Action. The undersigned requested the Examiner for clarification during the January 11, 2007 interview with the undersigned and with Supervising Examiner Andres, regarding the status of this rejection reason. Applicants thank the Examiner for withdrawing the obviousness double-patenting rejection over US 5,674,844, as indicated in the subsequent January 22, 2007 interview summary.

The Examiner states in the Office Action that claims 97, 99, 105-113 remains rejected for obviousness-type double patenting as being allegedly unpatentable over claims 1-8 of US 6,288,031, claims 1-2 of US 6,495,513, claims 1-16 of US 6,800,603 and claims 1-18 of 6,949,505, and that this rejection also applies to claims 112 and 113.

Without conceding to the correctness of the rejection, Applicants hereby submit a suitable terminal disclaimer. Applicants bring the Examiner's attention to a terminal disclaimer filed by the Applicants on May 17, 2005, disclaiming any term which would extend beyond the expiration date of US 6,288,031.

Applicants believe the argument above and the terminal disclaimer submitted herewith obviate the rejection reason. Therefore, Applicants respectfully request this rejection reason be withdrawn.

35 U.S.C. §112 First Paragraph

Claims 97, 99, and 105-113 were rejected under 35 U.S.C. §112 First Paragraph allegedly for not being enabled by the specification. The Examiner concedes that the claims are enabled for a method of decreasing neuronal death associated with a neuropathy or injury by administering to a subject a morphogen comprising a dimeric protein having fragments of amino acids 38-139 and 43-139 of SEQ ID NO:5 with homology as recited in claim 97. The Examiner then states that the specification does not provide enablement for such method with regard to all forms of neuropathy or injury, wherein the morphogen comprising any amino acid sequence of morphogens as recited in claim 97.

Without conceding the correctness of the Examiner's allegation, in the interest of advancing prosecution, Applicants have amended the claims to more specifically describe the characteristics of neuropathies and injuries that the claimed methods address. The support for the amendment can be found throughout the specification, but in particular, in the text found on page 6, lines 6 to 34; and page 15, lines 5 to 12.

It is clear from the claims themselves and the specification that the basis for the therapeutic effect of the morphogen to decrease cell death is at least in part due to the morphogen's ability to increase or sustain N-CAM and/or L1 isoform expression. See, for example, page 6 lines 6 to 34 for the state of the art regarding N-CAM and neuronal cell growth, differentiation and development, and Example 6 at page 76 line 1 to page 80 line 18 for the effect of morphogen on the production of L1 and N-CAM and, consequently, the survival of neural cell in vitro. Therefore, subjects with divergent neuropathies and injuries that are associated with neuronal cells that were impaired in N-CAM and/or L1 isoform activity, which in turn correlates with the lower survival rate of neuronal cells, would benefit from administration of a morphogen. The direct support for the amended language of claims 97 and 112 is found on page 79 at lines 20-27, and on page 80, lines 6 to 17. The amended claims more clearly describe this technical feature and specify such neuropathies and injuries.

Applicants also amended claims 98 and 113 to more clearly describe the chemical and physical injury that morphogen positively affects, and what was meant by "at risk of" in the previous claim language. No new matter was added by describing more concretely under what

conditions the neuronal cells are considered to be "at risk." Chemical injury, as contemplated in this application, occurs as a result of exposure of neurons to toxins that inhibit the proliferation and migration of neurons and that interfere with cell adhesion. To better describe what Applicants seek to claim, the claims were amended to recite exposure to toxins; injury may occur as a result of exposure in the absence of a morphogen. Applicants bring the Examiner's attention to the description in the specification regarding chemical injury and the risk of chemical injury upon exposure to a toxin, such as at page 12, line 30 to page 13, line 1 and in Example 5, starting at page 74, line 24 to page 75, line 30. The support for the amended language is found at page 74, line 35 to page 75, line 9.

With regard to physical injury, Applicants submit that the term "physical injury" is clearly understood by one skilled in the art. As to what neuronal cells may be at risk of physical injury, Applicants have amended claims 98 and 113 so that they now relate in part to anticipated physical injury due to surgery. The support for the amendment is found on page 15, lines 8 to 12.

With regard to the Examiner's contention that the specification only teaches using OP-1, Applicants respectfully traverse and submit that the specification gives ample guidance and description of the activities and structural features of any analog useful to practice this invention. Applicants point out to the Examiner that morphogens comprise a closely related family of proteins which are able to functionally replace one another *in vivo*. Applicants respectfully submit that the morphogen family was known in the art to have activities that allow substitution of one morphogen by another. See, for example, Padgett *et al.*, *Proc. Nat'l Acad. Sci. USA* 1993 Apr 1;90(7):2905-9. Accordingly, it would have been possible for one skilled in the art to practice the instant invention without undue experimentation based on an example provided in the specification. The Applicants also bring the Examiner's attention to page 39, lines 27 to 32, where U.S. Patent No. 5,011,691 (the "'691 patent") is cited to be incorporated by reference. The '691 patent shows that artificial sequences COP-1, COP-3, COP-4, COP-5, COP-7 and COP-16 were created from the consensus amino acids encompassing several naturally occurring morphogens. The '691 patent shows COP-5 and COP-7 proteins enhanced bone and cartilage formation *in vivo* in a manner analogous to naturally occurring OP-1. The sequences of the

seven cysteine domain of COP-5 and COP-7 both share approximately 78% homology with the OP-1 seven cysteine domain sequence, indicating these polypeptides fall within the scope of the claimed invention. Because they demonstrate similar physiological activity to OP-1, COP-5 and COP-7 are expected to behave similarly to OP-1 in other aspects of their morphogenic activity. Applicants submit that the incorporation by reference of COP protein data give further support to the scope of the claims.

The specification clearly describes morphogens as well as what Applicants consider to be functional equivalent of morphogens. See page 20 line 22 to page 41, line 22. These descriptions are clear and sufficient. The multiplicity of issued patents with precisely the same definition of morphogen in the claims is ample proof of this fact. Since the claimed morphogen is a well-defined agent, the amount of morphogen is disclosed, the parameters for treating the condition are disclosed, and the conditions themselves are disclosed, only routine experimentations are involved. Accordingly, Applicants submit that the disclosure in the specification meets Applicants' burden of showing how to practice the claimed subject matter.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Applicant believes no additional fee is due with this response. However, if any fee is due, please charge our Deposit Account No. 18-1945, under Order No. JJJ-P06-504 from which the undersigned is authorized to draw.

Dated: January 31, 2007

Respectfully submitted,

By _____

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